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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,085	03/02/2007	Bernard Verrier	033339/305755	9648

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EXAMINER	
THOMAS, TIMOTHY P	
ART UNIT	PAPER NUMBER
1628	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,085	VERRIER ET AL.	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2 and 4-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 4-9* is/are rejected.

7)☒ Claim(s) *9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/21/2010 has been entered.

Response to Arguments

2. Applicants' arguments, filed 1/21/2010, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

3. Applicant's arguments with respect to the rejection under 35 USC 102 or alternatively under 103 have been fully considered but they are not persuasive:

Claims 2 and 4-9 remain rejected under 35 U.S.C. 102(e) as anticipated by Vail, III et al. (US 7,150,888 B1; 2006; filed 2002 Sep; priority 2000, 2001, 2002) as evidenced by Swords et al. (“Composition of Australian Tea Tree Oil (Melaleuca alternifolia)”; 1978; Journal of Agricultural Food Chemistry; 26(3): 734-737); or, in the alternative, under 35 U.S.C. 103(a) as obvious over Vail, III et al. (US 7,150,888 B1; 2006; filed 2002 Sep; priority 2000, 2001, 2002) in view of Swords et al. (“Composition

of Australian Tea Tree Oil (Melaleuca alternifolia)"; 1978; Journal of Agricultural Food Chemistry; 26(3): 734-737).

The rejection is maintained for the reasons of record and the reasons that follow.

It is noted that independent claim 9 has been amended to use "comprising" language before the recited method step; however, line 5 recites administration of "a CFTR activating agent consisting of at least one linear n-alkanol…" The language "consisting of" is normally "closed" language, excluding other components. However, when followed by "at least" the language would be open language, where other components may be present. Additionally, claim 7, dependent upon and which would further limit claim 9, requires combination of a carrier with said n-alkanols, which indicates that the "consisting of at least one linear n-alkanol" language of claim 9 does not exclude the n-alkanol from being combined with other compounds, such as a carrier. The broadest reasonable interpretation of the "a CFTR activating agent consisting of at least one linear n-alkanol" language would require a linear n-alkanol as a component of the "agent", but other compounds, including compounds not identified as having CFTR activating properties (i.e., the other components of tea tree oil), are not construed to be excluded. Therefore, the administration of tea tree oil (or 99% tea tree oil with 1% eucalyptus oil), which contains about 40 ppm n-hexanol, by inhalation to individuals having cystic fibrosis is taken to meet the required step of the claimed method as amended.

Applicant argues the combination of Vail and Swords does not disclose or suggest the claimed invention, because each and every element of the claims has not

been disclosed; that Vail does not disclose or suggest a method of partially or fully activating cystic fibrosis transmembrane conductance regulator channels (CFTR) in epithelial cell membranes, that Vail relates to a different technical problem than the claimed invention; that Vail does not claim or show that eucalyptus oil or tea tree oil, or any of the various components thereof, have any effect upon defective CFTRs. It is acknowledged that the focus of Vail is to prevent respiratory system diseases. However, the claims require the step of administering to "said patient", i.e., a patient in need of treatment (a patient with cystic fibrosis satisfies the required "in need of treatment" patient population), whom suffers from at least one pathology associated with the non-activation of said CFTR (a cystic fibrosis patient would meet this "suffers from" limitation), a CFTR activating agent consisting of at least one linear n-alkanol in a specific amount. The administration of tea tree oil containing 40 ppm n-hexanol, an amount within the recited range of claim 8, is taken to satisfy the required amount limitation. When the required active component in the recited amount is administered to the same patient population, the partially or fully activating of CFTR channels would be a characteristic result of the same active step. The burden has been shifted to applicant to demonstrate the characteristic would not be the result. This burden has not been met.

Applicant argues that the language of amended claim 9 recites exclusively to a method wherein only an active ingredient consisting of at least one C_6-C_{10} alcohol, is administered to patients with defective CFTRs; that the administration of tea tree oil which comprises a complex mixture of several mainly phenyl group containing organic

compounds, to the lungs of a patient with defective CFTRs does not disclose or suggest the claimed method. The presence of the phenyl groups is not critical to the rejection basis, when the claim are construed that such compounds may be present along with n-hexanol, as discussed above. The record has demonstrated that Vail or Vail as evidenced by Swords does teach that tea tree oil administered would contain about 40 ppm n-hexanol, an amount within the range recited in claim 8, which would meet the required step of the claims.

Applicant argues that the combination of Vail and Swords does not disclose administering a CFTR activating agent consisting of at least one linear n-alkanol selected from the group consisting of C_6-C_{10}. This has been addressed above.

Applicant argues that the caustic nature of the phenyl containing compound is the reason why they have generalized antibiotic effects, which is the reason why Vail uses Tea Tree Oil to prevent and/or treat opportunistic infections of the human respiratory tract. This argument is speculation and has not been established by evidence on the record. MPEP 716.01 (c) (II) indicates the arguments of counsel cannot take the place of evidence in the record.

In fact, Vail clearly indicates that “one or more components from tea tree oil, (which are defined below)" may be used in the method (col. 9, line 66 – col. 10, line 1); the “components…defined below” specifically include hexanol (col. 14, lines 40 and 46). The point is that there is an embodiment taught by Vail that would include the administration of only hexanol to individuals with cystic fibrosis. This embodiment would not involve any phenyl containing compound, whether caustic or not.

Applicant argues that the administration of 40 ppm hexanol when administered to the patient via inhalation, generating in the vicinity of the epithelial cells of the patient a concentration of hexanol sufficient to activate, partially or fully, the CFTR is absurd; that the fact that Vail is concerned with exposing the respiratory tract to the vapor of Tea Tree Oil so as to provide an additional level of innate immunity to combat air borne pathogens; that the quantity of Tea Tree Oil inhaled to achieve this effect must be miniscule, even though this point is not taught or implied by Vail. Applicant theorizes that this would be the case so as not to prevent damage to the lungs by the various caustic compounds present in Tea Tree Oil. As discussed above, this point of the caustic nature of compounds has not been established. This argument is also not consistent with the disclosure of Vail, which indicates that because of lower cineole level, tea tree oil is less toxic and less irritating than eucalyptis oil (col. 18, lines 2-3); tea tree oil can safely be used in small doses on all mucous membranes...internal ingestion has been attempted without noticeable toxic effects (col. 17, lines 3-7); it is noted that rare adverse affects, e.g., in one out of 50 patients, have been reported, but the 49 remaining patients showed "remarkable improvement of the conditions being treated" (col. 17, lines 28-40). As is expected with most drugs, side effects do occasionally occur; however, such side effects would be outweighed by the benefit to the patients being treated. Furthermore, the discussion at col. 5, 3rd-4th paragraphs, indicates that deep inhalation of the tea tree oil was made with each nostril, with a number of repetitions was made, this was sometimes repeated every 30 minutes; the 5th paragraph indicates that "very strong vapors" were inhaled each time, and occasionally

the fluids themselves got sucked up into the nose (although undesirable to inhale a liquid). This indicates aerosol or a nebulized administration intranasally, identical to the administration routes recited in instant claims 6-7. This evidence from Vail is inconsistent with applicant's "miniscule amount" theory; in contrast, the teaching of Vail implies that the maximum amount that could be inhaled was administered repeatedly. Additionally the embodiment of administration of only hexanol, without the presence of other tea tree oil components, taught by Vail, would no involve miniscule amounts, but the same higher amount of n-hexanol would be the upper limit cutoff as would be used in the instant application, which would be established by weighing the benefit observed for the patient with potential side effects of a dose too high; clinical trials used to determine dose and balance safety and efficacy would be expected to arrive at the same amount for the Vail n-hexanol component dosed as for the instant claimed embodiment of n-hexanol being administered.

Applicant further argues the inventors have established that it is necessary to achieve a certain concentration around the target cell/defective CFTR, referencing Figure 2, (which shows efflux as a function of octanol, and does not have data for n-hexanol); that in particular the inventors have found that a concentration of 1 mM of octanol or more achieves optimal levels of CFTR activation; that as such the combination of Vail and Swords also does not teach a method that includes the step of administering to said patient a CFTR activating agent in the recited amount. It is noted that the claims do not require a 1 mM amount, and no amount has been established for n-hexanol, with the exception of the concentration range recited in claim 8. Since 40

ppm is above the minimum recited in claim 8, this amount is taken to satisfy the required amount of claim 9. Further, when n-hexanol is administered as the only compound, it would have been obvious to increase the amount used, and to optimize it for the purposes taught by Vail. Such an increased amount would also have been sufficient to meet the claimed amount limitation.

Applicant's crude calculations are not clear; and tend to render the amounts recited in claim 8 as confusing. 40 ppm n-hexanol in solution corresponds to about 0.39 mM n-hexanol, an amount greater that applicant argued 0.1 mM. Inhalation of this solution would be expected to result in similar concentrations at the lung surface, or about 0.39 mM in the vicinity of the epithelial cell membranes. This analysis is consistent with the lower concentration of claim 8, 10 ppm, which would give about 0.1 mM at the lung surface, the amount argued for by applicant. Furthermore, the amount of 40 ppm is within the range taught by claim 8; administration of a concentration that is the same via the same intranasal inhalation would result in the same amount in the vicinity of the epithelial cell membranes, as is required by claim 9. The burden has been shifted to applicant to demonstrate that this amount is not achieved. This burden has not been met.

Applicant argues that there is not support in the teachings of Vail and Sword to utilize hexanol in a purified form. This is not accurate. As discussed above, Vail clearly indicates that “one or more components from tea tree oil, (which are defined below)" may be used in the method (col. 9, line 66 – col. 10, line 1); the “components…defined below” specifically include hexanol (col. 14, lines 40 and 46). This is a teaching of

purified hexanol or hexanol in a carrier. This is a teaching of individual components of the Tea Tree Oil, including hexanol, in a purified form.

Applicant argues that one of skill in the art would not have seen any effect upon the CRTR due to the hexanol present according to Swords; that approaching this situation logically, would have lead to more prevalent components of Tea Tree Oil; that the fact that hexanol would have been chosen from all the other 48 components of Tea Tree Oil shows the obviousness objection is based on ex post facto analysis. This is not persuasive. Even if the claims were to be construed that the language of the claims excludes the additional components of Tea Tree Oil, Vail clearly indicates that one of the components may be used, and Vail names hexanol in the list of the components, rendering its use, even as the single active agent, as obvious. The fact that it is one component out of 48 is not sufficient to render it as nonobvious, especially when Vail clearly indicates that one component may be used. Carrying out administration of n-hexanol present using 40 ppm or a greater amount (which would have been obvious when using a purified component), to an individual with cystic fibrosis would have met the require step of the instant claims; even though Vail does not discuss the claimed mechanism of CFTR channel activation, while practicing the same method step, i.e., administration of n-hexanol, in haled from a solution containing 40 ppm or a greater amount, would have characteristically resulted in at least partially opening of at least one CFTR channel required by the method claimed.

Applicant argues that the examiner's estimation of hexanol being about 10% as abundant as α-Cubebene, based on the relative sizes of their peaks cannot be used as

there is no certainty that this estimate is correct and hexanol could be a smaller amount or just a contaminant. Since in GC the area under the peak is proportional to the relative concentration, this estimate is still considered to be accurate. Since a case has been made of the estimated amount based on the reported data, the burden is shifted to applicant to demonstrate this estimate is inaccurate. The Patent Office does not have laboratories and cannot measure the amounts of hexanol in concentrated Tea Tree Oil. Furthermore, Vail specifically names hexanol as a component, rendering it obvious to isolate and use in a pure form, at even higher amounts than would be estimated from Swords.

Applicant argues that although Swords states that Tea Tree Oil contains hexanol other sources do not; that if Vail were combined with ISO 4730 there would be no basis for use in the method of claim 9. This is not persuasive; Vail clearly indicates hexanol is a component of Tea Tree Oil at col. 14, line 46.

Claim Objections

4. Claim 9 is objected to because of the following informalities: Line 4 recites "comprising the steps…" (plural), but only one step (singular) (i.e., administering), follows this language; applicant is advised to amend "steps" to "step". Appropriate correction is required.

Conclusion

5. No claim is allowed.

6. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1628

/Brandon J Fetterolf/

Primary Examiner, Art Unit 1642